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ORIGINAL ARTICLE

Sleeve resections with unprotected bronchial anastomoses are safe even after neoadjuvant therapy†

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Abstract

OBJECTIVES: Sleeve resection is the operation of choice in patients with centrally located tumours, in order to avoid a pneumonectomy. Most surgeons protect the bronchial anastomoses with tissue to prevent insufficiencies. The purpose of this study is to report on outcome of unwrapped bronchial anastomoses, especially after neoadjuvant chemo- or chemoradiotherapy.

METHODS: Between 2000 and 2010, 103 patients [59 years (range 16–80), 40 females] underwent bronchial sleeve resections without coverage of the anastomosis with a tissue flap. We retrospectively reviewed the data for morbidity, mortality and survival, especially with regard to the type of resection, neoadjuvant therapy and stage.

RESULTS: Sleeve lobectomy was performed in 88, sleeve bilobectomy in 8, sleeve pneumonectomy in 4 and sleeve resection of the main bronchus in 3 patients. Twenty-seven patients had a combined vascular sleeve resection. Neoadjuvant chemotherapy was performed in 20 and radiochemotherapy in 5 patients. Non-small cell lung cancer (NSCLC) was present in 76 patients (squamous cell carcinoma in 44, adenocarcinoma in 24, large cell carcinoma in 6 and mixed cell in 2) and neuroendocrine tumour in 20 and other histological types in 7 patients. The pathologic tumour stage in NSCLC was stage I in 26, stage II in 26, stage IIIA in 16, stage IIIB in 7 and stage IV in 1 patient. There were no anastomotic complications, especially no fistulas. One patient developed narrowing of the intermediate bronchus without need for intervention. Twenty-four patients had early postoperative complications, including 11 surgery-related complications (air leakage, nerve injury, haemothorax or mediastinal emphysema). The 30-day mortality was 3% (one patient died due to heart failure and two with multiorgan failure). The 5-year survival rate was 63% in NSCLC patients and 86% in neuroendocrine tumour patients.

CONCLUSIONS: Sleeve resection without wrapping the bronchial anastomoses with a tissue flap is safe even in patients who underwent neoadjuvant chemo- or chemoradiotherapy. Therefore, wrapping of the bronchial anastomoses is not routinely mandatory.

Keywords: Sleeve resection • Neoadjuvant treatment • Anastomoses

THORACIC

INTRODUCTION

Since Price-Thomas [1] first introduced bronchial sleeve resection in 1947 and Allison [2] applied it for the treatment of a bronchogenic carcinoma in 1954, this procedure has gained a definite role in the treatment of centrally located bronchopulmonary neoplasms [3, 4].

Issues of concern that led to a gradual introduction of this technique into common surgical use included the possible risk of local recurrence and of disadvantage in long-term survival and the complications related to the bronchial anastomosis. Recent studies demonstrated that in sleeve resections, there is no evidence of increased risk of local recurrence after sleeve resection, and long-term survival is similar or better than after pneumonectomy. Furthermore, this technique can be performed with a low risk of bronchial anastomotic complications [5–9].

In order to obtain adequate blood support to the suture line and to prevent anastomotic complications, the coverage of the bronchial anastomosis with an autogenous tissue pedicled flap has become a common and recommended procedure [10]. The wrapping of the anastomosis has been described with pericardial, pleural or intercostal muscle flaps, with mediastinal fat, omentum or internal mammary artery pedicles [11–13].

Wrapping the bronchial anastomosis with either omentum or an internal mammary artery pedicle was also routinely performed in lung transplantations in the late 1980s and early 1990s, but several studies demonstrated that it is not mandatory for bronchial healing [14, 15].

In our centre, we routinely performed bronchial sleeve resections without wrapping the anastomosis, also in patients who

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had neoadjuvant chemo- or chemoradiotherapy. In this study, we retrospectively analysed the postoperative mortality, the long-term survival and the incidence of short- and long-term morbidity, especially with regard to the type of resection, neoadjuvant therapy and stage, in order to assess whether wrapping the bronchial anastomosis is still an essential procedure in course of sleeve resections or not.

PATIENTS AND METHODS

In this retrospective study, we included 103 consecutive patients who underwent bronchial sleeve resections without wrapping the anastomosis, between January 2000 and April 2010. Patients operated on cardiopulmonary bypass were excluded from this analysis.

There were 63 males and 40 females with a median age at operation of 59 years (range 16–80). The preoperative evaluation of the patients included physical examination, chest radiography, pulmonary function tests, blood examinations, electrocardiography, computed tomography (CT) of the chest and upper abdomen and positron emission tomography-CT (PET-CT). PET-CT-positive lymph nodes were examined through endobronchial ultrasonography (EBUS). Only if EBUS was negative and a high suspicion for lymph nodal metastases was present, mediastinoscopy was performed. Preoperative CT scans or bronchoscopy often identified a possible candidate for a sleeve resection, but the final decision was always taken intraoperatively.

All patients underwent a double-lumen tracheal intubation and a standard anterolateral thoracotomy. To evaluate the airway anatomy and the tumour invasion, flexible bronchoscopy was carried out immediately before and during the operation. The bronchus was divided with a sharp knife obtaining straight margins distant from the tumour. Frozen sections of the resected margins were analysed to ensure complete resection. The end-to-end bronchial anastomosis was performed using a continuous absorbable running 4–0 polydioxanone suture (Ethicon, Inc., Somerville, NJ, USA) on the membranous airway wall. The cartilaginous part was anastomosed with an interrupted suture technique, and the knots were placed outside the lumen and tied at completion of the anastomosis comparable to the technique in lung transplantation. Care was taken to keep the peribronchial tissue intact, and systematic lymph node dissection was carried out in all neoplastic patients. The wrapping of the anastomotic bronchial suture with any kind of autogenous tissue pedicled flap was not performed. When necessary, arterial sleeve resection was carried out, using a 5–0 polypropylene running suture (Prolene, Ethicon, Inc.). At the end of the procedure, the bronchial anastomosis was controlled with flexible bronchoscopy and cleaned up from clots and secretions.

The follow-up of the patients was started from the date of the operation to the time of death or to the last observation. Data were collected from the hospital database and, for those who were not routinely followed up, from the referring physicians, the patients themselves and their families.

Patient records were collected for age, gender, type of operation, histology, stage of the disease at operation time, neoadjuvant therapy, short- and long-term postoperative complications and survival. Postoperative mortality was considered as death within 30 and 90 days from the operation.

RESULTS

Out of 992 resections, sleeve lobectomy was performed in 88 patients, out of them 49 were of the right upper lobe, 28 of the left upper lobe, 6 of the left lower lobe and 5 of the middle lobe. Eight sleeve bilobectomies, four sleeve pneumonectomies and three main bronchus sleeve resections were also performed (Table 1). In 27 (26%) patients, a concomitant vascular sleeve resection was carried out.

Twenty-five (24%) patients received preoperative platinum-based induction therapy. All of these patients had neoadjuvant chemotherapy (two to six cycles), and five (20%) of them received concurrent chemoradiotherapy (three to six cycles of chemotherapy plus 44–66 Gy of radiotherapy).

Histological examination showed a non-small cell lung cancer (NSCLC) in 76 patients (squamous cell carcinoma in 44, adenocarcinoma in 24, large cell carcinoma in 6 and mixed cell in 2), a pulmonary neuroendocrine tumour in 20 (15 typical carcinoid tumours and 5 atypical carcinoid tumours) and other histological types in 7 patients (Table 2).

Among the 76 NSCLC patients, the TNM classification identified 26 stage I disease (10 IA and 16 IB), 26 stage II disease (9 IIA and 17 IIB), 16 stage IIIA disease, 7 stage IIIB disease and 1 stage IV disease (with resected synchronous brain metastasis).

Short- and long-term morbidity is shown in Table 3. There was no anastomosis-related complication, especially no fistulas. A total of 24 (23%) patients experienced 27 early postoperative complications. Three patients (3%) presented long-term complications, including two post-pneumonectomy syndromes, which were successfully treated with the implantation of prostheses, and one intermediate bronchus narrowing. This mild stenosis didn't need any surgical treatment, and the patient died after 23 months because of a pulmonary embolism.

The 30-day mortality was 2.9% (three patients) and the 90-day mortality was 4.8% (five patients). One patient died on the seventh postoperative day because of heart failure. Two patients died because of multiorgan failure: one on the 9th and one on the 22nd postoperative day. Two patients received adjuvant radiotherapy of the mediastinum and tree adjuvant chemotherapy. Eight patients developed a local recurrence during follow-up, out of them three patients had a completion pneumonectomy, two patients radiotherapy and three patients a second-line chemotherapy.

Table 1: Type of bronchial sleeve resection

Type of resection	No. of patients (%)
Lobectomy	88 (85.4)
Right upper lobe	49
Left upper lobe	28
Left lower lobe	6
Middle lobe	5
Bilobectomy	8 (7.8)
Upper	2
Lower	4
Right pneumonectomy	4 (3.8)
Main bronchus resection	3 (2.9)
Right	1
Left	2

Table 2: Histological diagnosis

Histology	No. of patients (%)
NSCLC	76 (73.7)
Squamous cell carcinoma	44
Adenocarcinoma	24
Large cell carcinoma	6
Mixed NSCLC	2
Pulmonary neuroendocrine tumours	20 (19.4)
Typical carcinoid tumours	15
Atypical carcinoid tumours	5
Other histological types	7 (6.7)
Metastases	3
Small cell carcinoma	2
Endobronchial lipoma	1
Sarcoma	1

Table 3: Short- and long-term complications

Type of complication	No. of patients
Short-term complications	27
Prolonged air leak	5
Laryngeal nerve palsy	2
Phrenic nerve palsy	1
Haemothorax	2
Mediastinal emphysema	1
Pneumonia	3
Atelectasis	1
Atrial fibrillation	8
ARDS	1
Sepsis	2
Heart failure	1
Long-term complications	3
Post-pneumonectomy syndrome	2
Bronchial stenosis	1

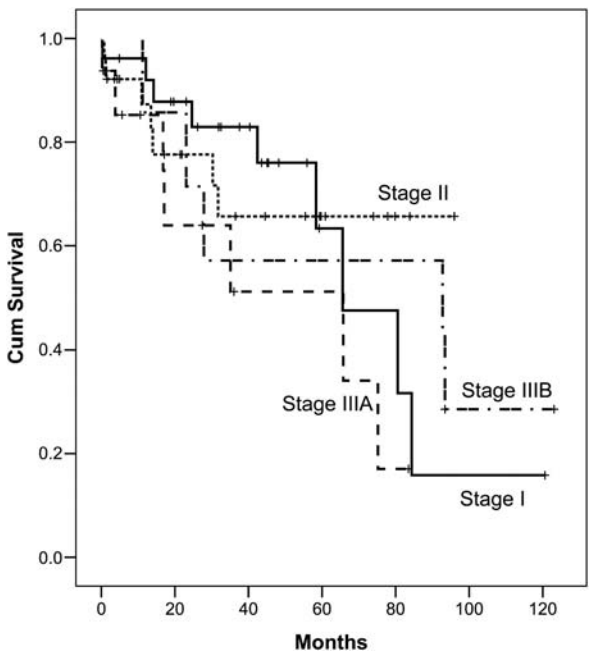

Figure 1: Survival curve related to stage in patients with NSCLC.

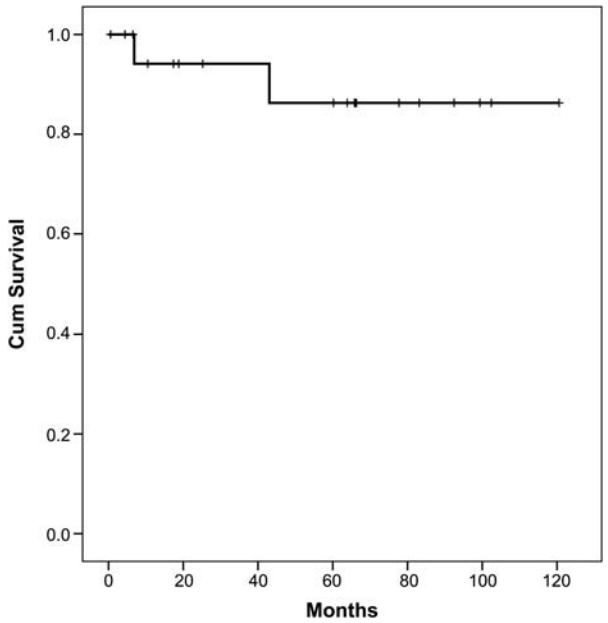

Figure 2: Survival curve in patients with neuroendocrine tumours.

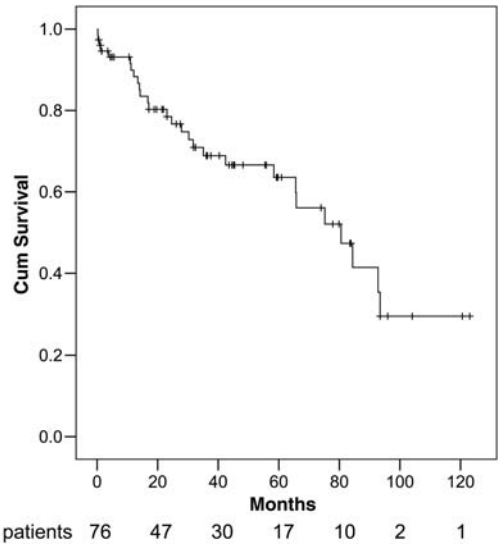

Figure 3: Survival curve in patients with NSCLC.

The mean postoperative hospitalization time was 9.7 days. Follow-up periods ranged from 1 to 123 months, with a mean of 41 months, and were complete for 102 patients (99%). There was one loss of follow-up after 2 months.

In the 76 NSCLC patients, the median survival was 81 ± 11 months (95% confidence interval: 59–102), and the 5-year survival rate was 63%. The 5-year survival rate in the 20 neuroendocrine tumour patients was 86% (Figs 1–3, computed Kaplan–Meier curves).

DISCUSSION

Bronchial sleeve resection has nowadays become an established alternative to pneumonectomy for patients with centrally located NSCLC, regardless of their pulmonary function. The

Table 4: Postoperative mortality, morbidity and long-term survival after sleeve resection with and without wrapping of the bronchial anastomosis

Study	No. of patients	Postoperative mortality (%)	Anastomotic complications (%)	5-year survival rate (%)	Wrapping
Kutlu and Goldstraw [20]	100	2	8	–	–
Rendina *et al.* [18]	145	3	2.7	37.9	+
Ludwig *et al.* [19]	116	4.3	6.9	39	+
Yildizeli *et al.* [17]	218	4.1	6.4	53	+
Rea *et al.* [12]	199	4.5	5.3	39.7	+
Yamamoto *et al.* [24]	201	1.4	3.3	57.8	±
Merritt *et al.* [13]	196	2	2	44	+
Konstantinou *et al.* [21]	45	2	0	57 (4-year survival)	–
Current study (Zurich)	103	2.9	1	63 (for NSCLC)	–

postoperative mortality and morbidity after sleeve lobectomy have been demonstrated to be equal or even better than after pneumonectomy, with a related better quality of life [5–9]. Bronchial sleeve resection is currently performed in ∼5–8% of patients with resectable lung cancer [16], but rates up to 13% have been reported [7].

In a recent meta-analysis, Ferguson and Lehman [8] reported a weighted mean operative mortality of 4.1% (confidence interval: 2.3–5.9%). Yildizeli *et al.* [17] also registered an operative mortality of 4.1% after sleeve resection, and Merritt *et al.* [13] had a 30-day mortality of 2%. In our study, we registered an overall 30-day mortality of 2.9%, which is in the lower range of literature (Table 4).

Sleeve resections are technically more demanding than standard lobectomies, and specific complications are related to the bronchial anastomosis. Its failure can lead to dehiscence and bronchopleural fistula, stenosis or bronchovascular fistula: situations that can often require completion pneumonectomy. The protection of the bronchial anastomosis is a subject of controversy. Many authors consider wrapping the bronchial anastomosis with an autogenous tissue pedicled flap as a fundamental procedure to reduce the incidence of severe anastomotic complications [18]. Though performing the wrapping of the bronchial anastomosis, Yildizeli *et al.* [17] reported an overall bronchial anastomotic complication rate of 6.4%, including bronchopleural and bronchovascular fistula, local necrosis and bronchial rupture. Merritt *et al.* [13] registered a bronchopleural fistula rate of 2%, and Ludwig *et al.* [19] reported a bronchial anastomotic insufficiency in 6.9% of their patients. In their series of 100 patients, Kutlu and Goldstraw [20] avoided the wrapping of the bronchial anastomosis and concluded that the careful handling of the airway, with the preservation of as much peribronchial tissue as possible, can avoid the need of any tissue flap on the bronchial anastomosis. Konstantinou *et al.* [21] routinely did not perform any wrapping of the bronchial anastomosis and registered no anastomotic complication. Accordingly, Rea *et al.* [22] did not find any significant difference in 30-day mortality between patients with or without pedicled flaps. Moreover, evidence has also been shown that, in the case of lung transplantation, the incidence of bronchial anastomotic complications is not affected by wrapping the anastomosis with either omentum or an internal mammary artery pedicle, since there is no improvement in bronchial healing [14, 15]. This concept could be adopted also for the anastomoses in course of sleeve resection. In our experience, we routinely did not use any kind of autogenous tissue pedicled flap and registered an anastomotic complication rate of 1%, consisting in an intermediate bronchus narrowing that didn't need any surgical treatment. We consider the preservation of an intact peribronchial tissue and a good experience in the field of bronchial anastomosis as the most important factors for a low anastomotic complication rate.

The safety of sleeve resection after induction therapy remains a concern. Neoadjuvant chemo- or chemoradiotherapy has been postulated to have a negative effect on bronchial blood supply, leading to an increased risk of anastomotic complications [23].

Rea *et al.* [12] found preoperative radiation as a significant risk factor for anastomotic complications, and Yamamoto *et al.* [24] demonstrated that bronchial healing is impaired after chemoradiation and more than after chemotherapy alone. In our series, 25 patients received preoperative induction therapy, all of them had neoadjuvant chemotherapy and 5 of them received concurrent radiochemotherapy. The most important complication associated with the use of a pedicled intercostal muscle flap is heterotopic calcification that can cause severe bronchial stenosis, as reported by Deeb *et al.* [25]. In our series, we observed no calcification and a narrowing of the intermediate bronchus didn't need any intervention.

Bronchial sleeve resection has been proved to achieve equal or better results, if compared with pneumonectomies, also regarding long-term survival [7, 8]. Yildizeli *et al.* [17] reported a 5-year survival rate of 53%, whereas Merritt *et al.* [13] and Ludwig *et al.* [19] reported an overall 5-year survival rate of 44 and 39%, respectively. Our 5-year survival rate was 63% in NSCLC (the lowest long-term survival rate for stage I disease is probably due to the small number of patients and the long observation period) and 86% in neuroendocrine tumours.

In conclusion, the postoperative mortality, the incidence of anastomotic complications and the long-term survival are comparable in patients who underwent bronchial sleeve resections with and without wrapping of the bronchial anastomosis. Sleeve resection without wrapping the bronchial anastomoses is feasible and safe in an experienced centre, even in patients who underwent neoadjuvant chemo- or chemoradiotherapy. Despite the limitation of our study due to the small number of patients after radiochemotherapy, we think that wrapping of bronchial anastomoses is not routinely mandatory.

Conflict of interest: none declared.

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EDITORIAL COMMENT

Wrapping of bronchial anastomoses: something of the past?

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Keywords: Lung cancer • Sleeve resection • TNM classification • Bronchial anastomosis

In this study, 103 patients who underwent a variety of sleeve resections in a centre of excellence are reported [1]. The reported 30-day mortality was 2.9% and 90-day mortality was 4.8%. Only one patient was lost to follow-up and the 5-year survival rate was 63% for the patients who were diagnosed with non-small cell lung cancer (NSCLC). Wrapping of the bronchial anastomosis with a pedicled tissue flap was not performed in this series. Only one patient developed a complication of the bronchial anastomosis without a need for specific intervention. No bronchial or bronchovascular fistulas were observed. The authors conclude that sleeve resection without wrapping of the bronchial anastomosis is a safe procedure, even after induction chemotherapy or chemoradiation.